

# On the scent of pleiotropy

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From bird songs to the great horn of the rhinoceros beetle, the gaudiest, and possibly most frequent, displays among animals occur in the context of sexual communication and reproduction. Testimony to the evolutionary importance of sexual communication is the recurring observation that signals are “tuned” to perception within species, and vice versa. The importance of sexual communication in coordinating mating interactions and determining successful outcomes has suggested to many that the mate recognition system of a species will be forever hovering around an optimally designed volley of information. A commonly held idea for how this coadaptation between signal and response might arise and be maintained has been dubbed the “coevolution” model, wherein genetically independent signal and response traits are mutually adjusted via selection on each component. An alternative model, often referred to as “genetic coupling,” surfaces regularly and hypothesizes a common genetic basis for both the signal and response. Under this model, both traits share genetic components. The appealing possibility that pleiotropic control assists the coordination of signaler and receiver traits, particularly during episodes of divergence and speciation, was fixed long ago within the scientific imagination (1–3) despite little evidence for it. The work presented in PNAS by Bousquet et al. (4) builds the best case to date for genetic coupling between signaler and receiver traits in sexual communication.

Using a combination of genetic techniques, Bousquet et al. (4) elegantly demonstrate that a single gene, *desaturase1*, plays a significant role in both the emission and perception of a pheromone in *Drosophila melanogaster*. Beyond providing evidence that signal and perception are influenced by the same gene, the authors provide expression and behavioral data that point to a possible mechanism by which the pleiotropic effects of this gene are mediated. Specifically, distinct regulatory regions drive tissue-specific expression of *desaturase1* in *D. melanogaster*, with expression targets in nonneuronal cells for pheromone synthesis and neuronal cells for pheromone perception.

## Disentangling coevolution and genetic coupling

The elaborate and conspicuous nature of sexual communication displays provided

inspiration for Darwin’s theory of Sexual Selection (5), paving the way for a rich legacy of study. Is it possible that the work by Bousquet et al. (4) represents the tip of an iceberg? Perhaps it does, but additional definitive examples of genetic coupling may continue to elude us. Both the genetic coupling and coevolution models predict a tight genetic correlation between the signal and response, which makes these models difficult to distinguish. In the case of genetic coupling, this correlation results

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from the shared genetic basis between signal and response. In the coevolutionary case, a genetic correlation can result from assortative mating or physical clustering of genes involved in signal and response. Thus, simply demonstrating that such a correlation exists is not sufficient to distinguish between these alternative models.

In addition, ascertainment bias may play a role, because it is easier to conclude decisively that traits do not share a common genetic basis. This can be shown, for instance, when the loci associated with signal and response map to different chromosomes or if the genetic correlation between the traits breaks down after several generations of controlled crosses. Indeed, case studies indicating an absence of genetic coupling abound. For instance, in several species of moth, including the almond moth (6), adzuki borer moth (7), corn borer moth (8), and heliothine moths (9, 10), it is quite clear that the female pheromone signal and male response are under separate genetic control. Similarly, male and female mating behaviors in *Drosophila arizonensis* and *Drosophila mojavensis* have distinct genetic bases (11), as do pheromone production and response in the pine engraver beetle (12).

Further, even when data are consistent with genetic coupling, it can be extremely challenging to rule out alternative hypotheses. Wing color and male color preference map to the same quantitative trait locus (QTL) region in *Heliconius* butterflies (13, 14), although it remains

unclear whether pleiotropy or tight linkage is at work. Similarly, in *Laupala* crickets, multiple QTLs underlie male signal variation, with female preference QTLs mapping to these same regions (15); again, the hypothesis of tight linkage vs. pleiotropy has not yet been tested. A single gene directly controls mating attractiveness in medaka fish, and although this gene also controls mating preference, it has not yet been demonstrated whether this control is direct or indirect (16). The report by Bousquet et al. (4) provides compelling empirical support for the genetic coupling model underlying chemical communication. A clear demonstration of genetic coupling in flies gives further credence to the possibility that genetic coupling may ultimately underlie the fine-tuning of signal and response in these other systems as well. It is compelling to ponder the future potential in these systems because they represent diverse taxonomic and diverse sensory examples in which genetic coupling might manifest.

## Looking ahead

The findings by Bousquet et al. (4), together with previous results, reveal that coadaptation between signal and response can evolve by either genetic coupling or coevolution (or some combination of both). A familiar companion to progress is that a suite of new questions arises. First, what are the relative frequencies of signal/response evolution being driven by coevolution vs. genetic coupling? Is the seeming overabundance of studies indicating a distinct genetic basis for signal and perception an artifact of the difficulty of demonstrating pleiotropic effects of single genes? Alternatively, do they reflect underlying biological reality? It is perhaps unsurprising that the first evidence clearly implicating genetic coupling in the evolution of signal and perception comes from an organism with almost unparalleled genetic and genomic tractability. With genetic tools and genomic resources continuing to emerge in non-traditional model systems, perhaps we will be poised to address this fundamental question in the very near future.

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Second, what conditions favor co-adaptation of signal and response via genetic coupling vs. coevolution? Is the evolutionary trajectory at all influenced by the mode of communication (i.e., acoustic, visual, chemosensory)? It has long been hypothesized that genetic architecture plays a major role in determining how the fine-tuning between signal and response can be maintained evolutionarily (2). In particular, it has been argued that when only a few loci serve as the genetic basis for either component of the communication process, genetic coupling is likely to predominate. This is because mutations in one of these few loci of large effect are likely to lead to large changes in phenotype; genetic coupling would greatly increase the probability of fixation of such mutations. In contrast, when signal and/or response is under polygenic control, coevolutionary dynamics might be the dominant mode of the evolution of communication. Empirical evidence in support of this hypothesis is lacking, although as we continue to dissect the genetic bases of signal and response in a variety of taxa with increased precision, we are sure to shed light on the role of genetic architec-

ture in coordinating sexual signaling. Understanding the genetic basis of several modes of communication is crucial to gain insight into whether different modalities have characteristic genetic architectures. It is possible that chemical signals/responses have their genetic basis in a few genes of major effect, whereas acoustic communication tends to be polygenically controlled, for instance (17). Much work is needed to understand further how and under what circumstances genetic coupling might be common and when coevolutionary dynamics are to be expected.

Beyond the context of the evolution of signal and response, the findings presented by Bousquet et al. (4) bear directly on a growing body of literature on pleiotropy. Pleiotropy describes the phenomenon by which a single gene affects more than one trait, although the mechanisms by which these effects are achieved have been debated. Two major avenues through which pleiotropic effects might manifest have been proposed: multiple functions of a single gene and multiple phenotypic consequences of a single molecular function. Multifunctionality of a single gene can, in principle, be mediated by alterna-

tive transcripts, RNA editing, tissue-specific expression, developmental stage-specific expression, or multiple functions of a single gene product. Multiple phenotypic consequences of a single molecular function, in turn, can be mediated by a single gene performing the same function in multiple pathways, for instance. The results from the study by Bousquet et al. (4) provide a beautiful example of the former, in which a single gene product has distinct functions in different tissues. Yeast provides an excellent example of the latter: The glutamine amidotransferase HIS7 functions in both histidine biosynthesis and purine nucleotide monophosphate synthesis (e.g., 18). Although it appears that pleiotropy in yeast is largely driven by multiple effects of a single molecular function (19), it remains unknown whether this is a general feature of pleiotropy across taxa. Future studies on genome-level patterns of pleiotropy as well as careful dissection of molecular functions of individual genes incorporating both spatial and temporal variation in expression in a variety of taxa are required to gain further insights into the relative importance of these two types of pleiotropy.

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